

SYMBOL	AMINO ACID
Y	L-tyrosine
G	glycine
F	L-phenylalanine
M	L-methionine
A	L-alanine
S	L-serine
I	L-isoleucine
L	L-leucine
T	L-threonine
V	L-valine
P	L-proline
K	L-lysine
H	L-histidine
Q	L-glutamine
E	L-glutamic acid
W	L-tryptophan
R	L-arginine
D	L-aspartic acid
N	L-asparagine
C	L-cysteine

FIG. 1

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SEQ ID. NO. 1 =

N-terminal D I C N T M H Y T N W T H I Y I C E E C-terminal

SEQ ID. NO. 2 =

N-terminal H K S A I V T L T Y D S E W Q R C-terminal

SEQ. ID. Nos. 1 and 2, denoted by underlining, are attributed to the E2 coding region of HPV-16 as follows:

5	10	15	20	25	30
1 M E T L C Q R L N V C Q D K I L T H Y E N D S T D L R D H I					
31 D Y W K H M R L E C A I Y Y K A R E M G F K H I N H Q V V P					
61 T L A V S K N K A L Q A I E L Q L T L E T I Y N S Q Y S N E					
91 K W T L Q D V S L E V Y L T A P T G C I K K H G Y T V E V Q					
121 F D G <u>D I C N T M H Y T N W T H I Y I C E E</u> A S V T V V E G					
151 Q V D Y Y G L Y Y V H E G I R T Y F V Q F K D D A E K Y S K					
181 N K V W E V H A G G Q V I L C P T S V F S S N E V S S P E I					
211 I R Q H L A N H P A A T H T K A V A L G T E E T Q T T I Q R					
241 P R S E P D T G N P C H T T K L L H R D S V D S A P I L T A					
271 F N S S H K G R I N C N S N T T P I V H L K G D A N T L K C					
301 L R Y R F K K H C T L Y T A V S S T W H W T G H N V K <u>H K S</u>					
331 <u>A I V T L T Y D S E W Q R D Q F L S Q V K I P K T I T V S T</u>					
361 G F M S I					

FIG. 2

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SEQ ID. NO. 3 =

N-terminal P T L H E Y M L D L Q P E T T D L Y C Y E Q L N D S S E E E C-terminal

SEQ ID. NO.4 =

N-terminal C D S T L R L C V Q S T H V D I R T L E C-terminal

Sequence ID. Nos. 3 and 5, denoted by underlining, are attributed to the E7 coding region of HPV-16 as follows:

	5	10	15	20	25	30
1	M H G D T <u>P T L H E Y M L D L Q P E T T D L Y C Y E Q L N D</u>					
31	<u>S S E E E D E I D G P A G Q A E P D R A H Y N I V T F C D K</u>					
61	<u>C D S T L R L C V Q S T H V D I R T L E D L L M G T L G I V</u>					
91	C P I C S Q K P					

FIG. 3

SEQ ID. NO. 5 =

N-terminus E K T G I L T V T Y H S E T Q R T K F C-terminus

SEQ ID. NO. 5, denoted by underlining, is attributed to the E2 coding region of HPV-18 as follows:

5	10	15	20	25	30
1 M Q T P K E T L S E R L S C V Q D K I I D H Y E N D S K D I					
31 D S Q I Q Y W Q L I R W E N A I F F A A R E H G I Q T L N H					
61 Q V V P A Y N I S K S K A H K A I E L Q M A L Q G L A Q S R					
91 Y K T E D W T L Q D T C E E L W N T E P T H C F K K G G Q T					
121 V Q V Y F D G N K D N C M T Y V A W D S V Y Y M T D A G T W					
151 D K T A T C V S H R G L Y Y V K E G Y N T F Y I E F K S E C					
181 E K Y G N T G T W E V H F G N N V I D C N D S M C S T S D D					
211 T V S A T Q L V K Q L Q H T P S P Y S S T V S V G T A K T Y					
241 G Q T S A A T R P G H C G L A E K Q H C G P V N P L L G A A					
271 T P T G N N K R R K L C S G N T T P I I H L K G D R N S L K					
301 C L R Y R L R K H S D H Y R D I S S T W H W T G A G N E K T					
331 <u>G I L T V T Y H S E T Q R T K F</u> L N T V A I P D S V Q I L V					
361 G Y M T M					

FIG. 4

TABLE 1. Serum Immunoassays Employing Peptides of Invention. These assays are compared against Pap cytology and HPV DNA Hybrid Capture analyses of cervical cells from the same patients. Serum and cervical cells were taken from participants by a gynecological physician. Pap smears and the Digene HPV DNA Assays¹ were processed at a certified clinical laboratory. Prior to completion of this trial, persons doing the Impact Diagnostics HPV Immunoassay were not informed of the results of other assays or of participant histories. Unless otherwise specified, participants were more than 35 years old. Key: pos = positive; neg = negative; n/a = not applicable or not done; insufficient = insufficient number of cells for analysis

<u>Sample</u>	<u>Digene HPV</u>		<u>Impact HPV Immunoassay²</u>			<u>Comments</u>
	<u>Pap Smear</u>	<u>DNA Assay</u>	<u>HPV-16a</u>	<u>HPV-16b</u>	<u>HPV-18</u>	
1	neg	n/a	pos	pos	neg	CERVICAL CANCER diagnosed in 1987;
2	n/a	n/a	pos	pos	pos	CERVICAL CANCER diagnosed in
3	neg	neg	pos	neg	pos	Previous Pap Smear – CIN III ³
4	neg	neg	pos	neg	pos	Previous Pap Smear – CIN III ³
5	neg	Insufficient	neg	neg	pos	Previous Pap Smear – CIN I ³
6	neg	neg	neg	pos	pos	Previous Pap Smear – CIN I ³
7	neg	neg	pos	pos	pos	Previous Pap Smear – CIN I ³
8	neg	neg	pos	neg	pos	Previous Pap Smear – CIN I-II ³
9	neg	neg	neg	neg	pos	No history of abnormal Pap Smears;
10	neg	neg	pos	pos	neg	No history of abnormal Pap Smears
11	neg	neg	pos	pos	pos	No history of abnormal Pap Smears;
12	neg	neg	pos	pos	pos	No history of abnormal Pap Smears
13	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
14	neg	neg	neg	neg	pos	No history of abnormal Pap Smears
15	ASCUS ³	pos	pos	pos	neg	No history of abnormal Pap Smears

TABLE 1. Serum Immunassays Employing Peptides of Invention. Continued

Digene HPV	Impact HPV Immunoassay ²					
<u>Sampl</u>	<u>Pap Smear</u>	<u>DNA Assay</u>	<u>HPV-16a</u>	<u>HPV-16b</u>	<u>HPV-18</u>	<u>Comments</u>
16	neg	neg	pos	pos	neg	No history of abnormal Pap Smears
17	n/a	n/a	pos	neg	neg	Promiscuous woman
18	n/a	n/a	pos	neg	neg	Promiscuous woman
19	neg	neg	neg	neg	neg	Virgin - 14 years old
20	neg	neg	neg	neg	neg	Virgin - 15 years old
21	neg	n/a	neg	neg	neg	No history of abnormal Pap Smears;
22	neg	neg	neg	neg	neg	No history of abnormal Pap Smears;
23	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
24	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
25	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
26	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
27	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
28	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
29	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
30	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
31	neg	neg	neg	neg	neg	No history of abnormal Pap Smears

¹The Digene HPV DNA Assay requires a substantial number of cells for successful detection of HPV DNA. Also, it only finds HPV DNA when the virus is abundantly proliferating (and not when infections are dormant).²HPV-16a = Epitope for the E2 Region of HPV-16; HPV-16b = Epitope for the E7 Region of HPV-16; HPV-18 = Epitope for the E2 Region of HPV-18. For the HPV Immunoassay, a positive result is visually expressed by a prominent BLUE color and a negative one by remaining COLORLESS.ASCUS refers to unusual or atypical cells in a Pap Smear. These are usually of undetermined significance and most often turn out to be inconsequential. In *mild dysplasia* (CIN I), only a few cells are abnormal, while in *moderate dysplasia* (CIN II) the abnormal cells involve about one-half of the thickness of the surface lining of the cervix. In *severe dysplasia* or *carcinoma-in-situ* (CIN III), the entire thickness of cells is disordered, but the abnormal cells have not yet spread below the surface. *Carcinoma-in-situ* means "cancer in place". If this condition is not treated, it often will grow into *invasive cancer*. In dysplasia and carcinoma-in-situ all of the abnormalities are confined to the surface lining (or "skin") of the cervix. For invasive cancer, the cells are not only disordered throughout the entire thickness of the lining, but they invade the tissue underlying the surface.